Proceedings – 23rd Annual Conference – IEEE/EMBS Oct.25-28, 2001, Istanbul, TURKEY

DIAGNOSIS OF SUB-CLINICAL VARICOCELE BY MEANS OF INFRARED FUNCTIONAL IMAGING

Arcangelo Merla[1,3], Andrea Ledda[4], Luigi Di Donato[1], Gian Luca Romani[1,2,3]

[1] Department of Clinical Sciences and Bioimaging, University of Chieti, V.le dei Vestini 13, I-66013 Chieti Scalo (Ch), Italy
[2] ITAB, Institute for Advanced Biomedical Technologies, V.le dei Vestini 13, I-66013 Chieti Scalo (Ch), Italy
[3] INFM, Sezione de L'Aquila, Italy
[4]Pierangeli Clinic, Pescara, Italy

Abstract – **Infrared Functional Imaging (IRFI) was used to detect sub-clinical varicocele. The evaluation of varicocele related hyperthermia and the different thermal properties of healthy and unhealthy testicles were used to detect the presence of the disease. A mild cold thermal stress performed on the scrotal region highlighted differences in the thermal recovery between the contralateral testicles and pampiniform plexuses . Mismatches in the equilibrium temperatures and in the recovery curves were used as objective parameters to infer the presence of varicocele, in a sub-clinical stages. 60 subjects, without any previous varicocele related symptoms, underwent the IRFI. 22 subjects out of the 60 showed abnormal values of the chosen parameters; clinical and Echo-Color-Doppler examination confirmed the presence of a sub-clinical first or second degree varicocele.**

***Keywords* – Infrared Imaging, varicocele, thermal recovery**

I. INTRODUCTION

The varicocele is a dilatation of the pampiniform venous plexus and the internal spermatic vein. Varicocele is the most widespread andrological disease and also the most frequent cause of infertility in men [1]. Dilatation of testicular veins due to venous incompetence in the pampiniform plexus (and/or in the spermatic veins) reduces the venous return in the scrotum, causing a stagnation of flood and venous hypertension, edema and thus increasing the testicular temperature [1].

Varicocele is considered the most important cause of chronic testicular heating. The vascularization of the testicle has two main roles: transportation and mobilitation of endocrine factors and metabolites and regulation of testicular temperature. In normal men the testicular temperature is about 3-4 °C below core body temperature and about 1.5-2.5 °C below the temperature of scrotal skin [2]. For the maintenance of a lower temperature the testicle relies on two thermoregulatory processes. Heat can be transferred to the external environment through the scrotal skin, since this is very thin, it hardly possesses any subcutaneous fat tissue, and has a very large surface. The second regulatory system is the pampiniform plexus. In this system the convoluted testicular artery is surrounded by several veins coiling around the artery several times. Arterial blood arriving at the testicle is thereby cooled down by the surrounding venous blood. The varicocele may therefore increase the testicular temperature. Such a testicular hyperthermia can results in a damage of the spermatogenetic function of the testicle [3].

Recently, Echo-Color-Doppler (ECD) has proved to be a powerful tool for evaluating varicocele and all other pathological scrotal conditions including lesions resulting from trauma, ischaemia, tumors, and inflammations.

On the other hand, the venous stasis associated with the presence of a varicocele may cause an increase in the temperature of the affected testicle and/or of the pampiniform plexus: therefore, an abnormal temperature difference between the two emiscrota may suggest the presence of a varicocele [2]. Telethermography (TTG) has been used to detect an abnormal temperature difference between the two testicles by several groups in the past [2]. However, the venous stasis induced by varicocele may affect the overall thermoregulation capability of the scrotum itself. In the present study we used DDTT, henceforth referred to as Infrared Functional Imaging (IRFI) to study the static and dynamic thermal properties of testicles in a population of asymptomatic "normal" subjects, with the aim at identifying the presence of a subclinical varicocele and at classifying its stage.

II. MATERIALS AND METHOD

60 volunteers (age 18÷27, average 21±2 yrs), that issued their informed consent and that

- did not have a previous clinical history of varicocele
- were negative to the clinical evaluation performed at the time of the military recruitment,

were examined according to the following protocol approved by the Ethical Committee: after clinical examination, both EcoColorDoppler (ECD) and IRFI analyses were performed to ascertain the presence of a sub-clinical varicocele. The ECD test, used as a gold standard method, was carried out by means of a ATL 5000 ECD system. The IRFI recording was performed using a 14 bit Digital TeleThermographic Camera AEG Aim 256 PtSi, 8-14 μm, 0.02 sec time resolution, 0.1 K temperature sensitivity. The temperature noise of the camera was reduced down to about 0.02 K by averaging each time 31 images taken at the maximum acquisition speed (31 images/sec).

The IRFI recording procedure consisted in recording:

- scrotal images of the subject; this permitted to detect the basal temperature T at the level of the pampiniform plexuses (T_p) and at that of the testicles (T_t);

Report Documentation Page

Report Date	Report Type	Dates Covered (from... to)
25 Oct 2001	N/A	-

Title and Subtitle Diagnosis of Sub-Clinical Varicocele by Means of Infrared Functional Imaging	**Contract Number**
	Grant Number
	Program Element Number
Author(s)	**Project Number**
	Task Number
	Work Unit Number
Performing Organization Name(s) and Address(es) Department of Clinical Sciences and Bioimaging University of Chieti V.le dei Vestini 13, I-66013 Chieti Scale (CH), Italy	**Performing Organization Report Number**
Sponsoring/Monitoring Agency Name(s) and Address(es) US Army Research, Development & Standardization Group (UK) PSC 802 Box 15 FPO AE 09499-1500	**Sponsor/Monitor's Acronym(s)**
	Sponsor/Monitor's Report Number(s)

Distribution/Availability Statement
Approved for public release, distribution unlimited

Supplementary Notes
Papers from 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Oct 25-28, 2001, held in Istanbul, Turkey. See also ADM001351 for entire conference on cd-rom, The original document contains color images.

Abstract

Subject Terms

Report Classification unclassified	**Classification of this page** unclassified
Classification of Abstract unclassified	**Limitation of Abstract** UU

Number of Pages
4

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- thermal recovery curves after cold thermal stress of the scrotum. Each recording consisted in a 5 minutes pre-stress period and in a 20 minutes post stress period, taking an averaged image every 30 seconds.

The thermal stress (*cold patch*) was performed through a cold dry patch at 10 °C lower than the basal scrotal temperature applied for 2 minutes onto the scrotum. To avoid environmental temperature related effects, the protocol forecasted an acclimation time not shorter than 20 minutes in the measurement room which temperature was maintained in the range (23 ±0.5) °C.

The subjects were sat during the IRFI evaluation.

Since the presence of varicocele may alter the normal thermophysical properties of the testicle and pampiniform plexus – especially the heat capacity, the tissue/blood ratio mass density and the heat carried out by blood flow -, we can use a heat balance equation to describe the local thermal effects associated with the disease. The basic idea of this work is to use parameters derived from that equation to possibly detect and classify the kind and stage of the disease. Furthermore, abnormal thermoregulatory properties with respect to those of a normal scrotum – or an asymmetric behavior between the two emiscrota - can be enhanced by a short time cold stress. On the basis of the local heat balance equation, the re-warming exhibited by the two emiscrota at level of the testicle site and of the pampiniform plexus can be characterized by means of the recovery time needed to return to the pre-cooling temperature: in fact this time directly depends on the thermophysical properties of the scrotum and on its blood perfusion [4]. In particular, we chose as a relevant parameter the time constant τ of the exponential function representing the best fit of the rewarming curve [4-5]. Fig. 1 shows an example of a rewarming curve of a normal testicle, of the exponential fit and a graphic representation of the time constant τ.

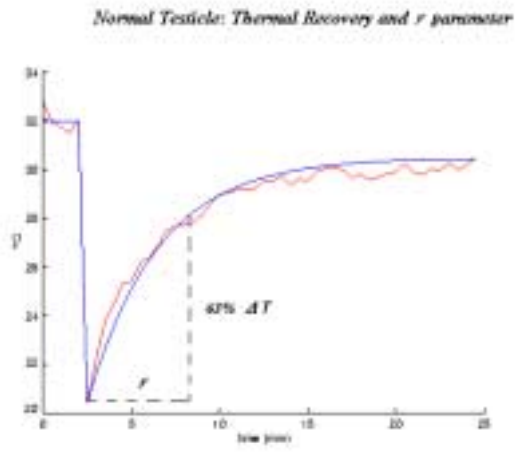

Fig. 1. Recovery after thermal stress on a normal testicle (red line). The time course of the testicle temperature exhibits an exponential pattern (blue lines) that can be described by means of the time constant τ.

Data analysis consisted in evaluating the basal pre-stress temperature and the recovery time constant τ at the level of the pampiniform plexus (T_p and τ_p, respectively) and at the level of the testicular site (T_t and τ_t, respectively) on each emi-scrotum. Basal scrotal temperature greater than 32 °C at the level of the testicular sites and basal scrotal temperature at level of the pampiniform plexus greater than 34 °C were estimated as a warning threshold [2]. Moreover, differences between the two testicles or the two pampiniform plexuses basal temperatures (ΔT_t and ΔT_p, respectively) greater than 1.0 °C were also estimated as a warning threshold. Finally, $\Delta\tau_p$ and $\Delta\tau_t$ values larger than 1.5 minutes were considered as a warning threshold as well, since so large $\Delta\tau$ could represent significant differences in the thermal recovery of the two emi-scrotum .

Abnormal values of T_p, T_t, τ_p, τ_t, $\Delta\tau_p$ and $\Delta\tau_t$ were considered as an indication of a possible varicocele for the testicle that had exhibited a faster rewarming [6]. Classification of different stages of the disease was successively attempted on the basis of the evaluated data set, and the results were blind checked with those obtained with ECD and clinical examination.

Analysis of data

The imaging and data analysis software was home made in a Matlab platform. The thermographic data were analysed by ANOVA, the statistical significance of which was fixed to $p< 0.01$. The statistical software package was the Matlab Statistics Toolbox.

III. RESULTS

No warning threshold in the basal temperatures was reached in 38 subjects. Moreover, they did not exhibit significantly different thermal recoveries between the two emi-scrota (see Table 1 and Fig. 2). Therefore they were classified as (IRFI) normals. Clinical examination and ECD study closely confirmed the absence of any stage of varicocele ($p<0.01$). 22 subjects out of 60 had one or more parameters larger than the respective warning threshold. Clinical examination and ECD confirmed the presence of a varicocele at several stages ($p< 0.01$) in all the 22 subjects.

The table 1 reports the results of the IRFI study and the average values of the chosen parameters with reference to each group of subjects that exhibited the same kind of thermal recoveries and basal skin thermal distribution. V1, V2 and V3 stand for first, second and third grade varicocele.

No false positive or false negative were found, so all the subjects that resulted IRFI positive were found positive when underwent clinical examination and the ECD exam as well. The statistical analysis (Table 2) highlighted that the best discriminant IRFI data between normal and pathological testicles were those expressing the comparison of the controlateral sides of the scrotum, both pre-stress (ΔT_t and ΔT_p) and dynamic ones ($\Delta\tau_t$ and $\Delta\tau_t$) .

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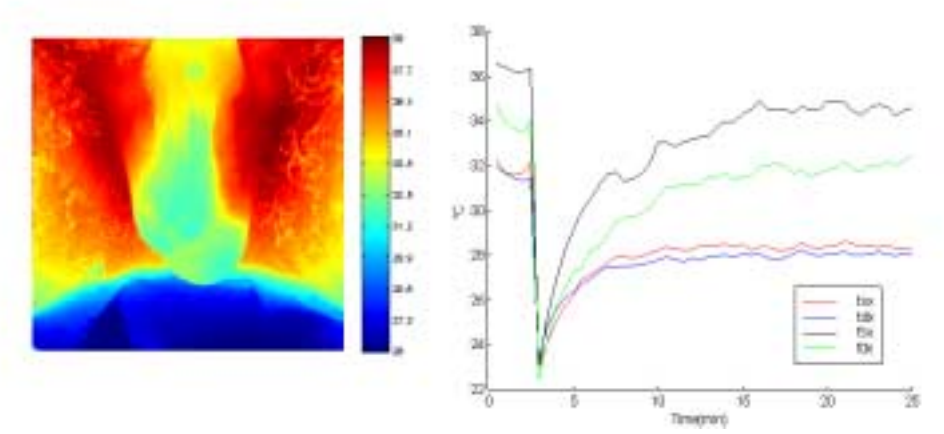

Fig. 2. First grade left varicocele. The pre-stress thermal distribution reports an hyperthermic area ($\Delta T_p > 1$ °C) onto the left plexus, while no significant differences are reported at level of the two testicles. Moreover, T_p of the left hemi scrota is greater than the warning threshold, while both the T_t are close to the warning threshold. The response to the cold stress higlights a faster rewarming of the left pampiniform plexus - black curve - with respect to the contralateral one – green curve- ($\Delta\tau_p > 1{,}5$ min). There are no remarkable differences between the rewarming curves of the two testicles (red and blue curves).

Table I: Results. IRFI Diagnostic hypothesis versus ECD and Clinical findings

Number of Subjects	T_t **(°C)**	T_p **(°C)**	ΔT_t **(°C)**	ΔT_p **(°C)**	$\Delta\tau_t$ **(min)**	$\Delta\tau_p$ **(min)**	*IRFI Diagnostic Hypothesis*	***ECD and Clinical findings***
38	< 32	< 34	*< 1.0* (0.5 ± 0.3)	*< 1.0* (0.4 ± 0.3)	*< 1.5* (0.5 ± 0.5)	*< 1.5* (0.5 ± 0.4)	*Negative*	*Negative*
8	*< 32*	*< 34*	*> 1.0* (0.8 ± 0.4)	*> 1.0* (1.6 ± 0.5)	*< 1.5* (0.5 ± 0.5)	*> 1.5* (2.0 ± 0.6)	*Positive* V1	*Positive* V1
5	*< 32*	*< 34*	*> 1.0* (0.7 ± 0.4)	*< 1.0* (0.6 ± 0.5)	*> 1.5* (2.0 ± 0.5)	*< 1.5* (1.0 ± 0.5)	*Positive* V1	*Positive* V1/V2
7	*> 32*	< 34	*> 1.0* (0.9 ± 0.4)	*> 1.0* (2.1 ± 0.6)	*< 1.5* (1.0 ± 0.5)	*> 1.5* (1.5 ± 0.5)	*Positive* V1/V2	*Positive* V2/V3
2	*> 32*	> 34	*> 1.0* (2.5 ± 0.4)	*> 1.0* (2.3 ± 0.5)	*> 1.5* (2.5 ± 1.0)	*> 1.5* (2.5 ± 0.5)	*Positive* V2/V3	*Positive* V3

Table I summarizes the overall results and the diagnostic hypothesis made on the basis of IRFI examination.

Table II: Results. ANOVA of the IRFI parameters: Normal Testicles versus Pathological Testicles

Parameter	**Average Values for Normal Testicles**	**Average Values for Pathological Testicle**	**ANOVA test**
T_t *(°C)*	30.4 ± 1.9	32.2 ± 2.0	p < 0.05
T_p *(°C)*	32.1 ± 2.0	34.6 ± 1.7	p < 0.05
ΔT_t *(°C)*	0.5 ± 0.3	1.0 ± 0.4	p < 0.01
ΔT_p *(°C)*	0.4 ± 0.3	2.3 ± 0.4	p < 0.01
τ_t *(min)*	*9.7 ± 6.0*	8.1 ± 4.7	*p < 0.1*
τ_p *(min)*	*6.3 ± 5.9*	4.4 ± 1.3	*p < 0.1*
$\Delta\tau_t$ *(min)*	*0.5 ± 0.5*	1.2 ± 0.4	*p < 0.001*
$\Delta\tau_p$ (min)	0.5 ± 0.4	1.7 ± 0.5	p < 0.001

IV. DISCUSSION

Varicocele is the most widespread andrological disease and also the most frequent cause of infertility in men. Although the gold-standard technique commonly added to clinical examination for assessment and classification of the disease is ECD, TTG has also been used in the past by several groups [6 – 11]. TTG has proved to be useful in providing noninvasive data on the absolute temperature of the scrotum, as well as on the temperature difference between the two testicles. A simple TTG investigation, however, although able to provide useful information, has not shown so far specific ability to infer the degree of the disease.

The experimental data reported in the present paper demonstrate that a first indication of the possible presence of varicocele is provided by an abnormal basal temperature of the testicles (9 out of 22 cases); a much stronger discrimination is obtained when the relative difference in the temperature of the two testicles and/or of the two pampiniform plexuses is measured. In this case, indeed, 17 out of 22 subjects had an abnormal ΔT_t, whereas all 22 subjects had abnormal ΔT_p. Since the whole population studied consisted in totally asymptomatic subjects, this first finding demonstrated that IRFI can be regarded as a powerful tool to perform a fast, non invasive, and economic screening on males in post-puberal age to prevent occurrence of asymptomatic varicocele, that may turn to be one of the most important cause of male infertility.

Furthermore, an increased blood reflux may alter the thermoregulatory capacity of the gonads. If this hypothesis is correct, a dynamic examination performed by means of the stress test can provides further elements that may be used for classification of the disease degree. The results obtained seem to confirm that a different thermoregulatory is associated to varicocele induced alteration of the blood flow. That this may also involve an abnormal functioning of the autonomic nervous system, or is more simply associated with a reduction of the heat transfer capability of the blood flow itself is still to be clarified and will be object of further investigation. In any case the dynamic parameters obtained from the thermal stress test seem to be more statistically significant with respect to the static ones. The thermal stress strongly enhances the different capability of thermoregulation of the affected testicle or of the affected pampiniform plexus as well. Whereas the absolute value of τ cannot be definitely associated to a specific degree of varicocele due to its large inter-individual variability, $\Delta\tau_t$ and $\Delta\tau_p$ appear more relevant parameters to a proper classification of the degree of the disease. In fact, when either of those parameters is beyond the threshold, a V1-V2 degree is suggested, and independently confirmed by the other clinical studies; when both parameters are beyond the threshold, a V3 degree is suggested and this hypothesis is confirmed by ECD.

The findings obtained by IRFI, clinical examination, and ECD were closely consistent. In particular, IRFI described consistently the pathological scene, highlighting 22 cases of sub-clinical varicocele.

Although our preliminary results are based on a limited number of cases, it emerges that it might be possible to classify the degree of varicocele through the parameters characterizing the thermal recovery in our study, namely $\Delta\tau_t$ and $\Delta\tau_p$. Further investigation on a wider population is necessary to validate this hypothesis.

It's likely that such a diagnostic approach may fail in the diagnosis of a bi-lateral, same degree varicocele, because in this case no differences would be observed either in the basal temperature or in the thermal recovery parameters. This limitation might be overcome by means of a very large casuistry devoted to create a normative database regarding both the basal scrotal temperature and the thermal recovery parameters.

In conclusion, IRFI may provide significant information to the investigation of varicocele, particularly in the sub-clinical phase, where no symptoms are often noticed by the patient. Moreover, by means of the rewarming curves, IRFI may give additional information about the thermoregulation properties of the testicles and, consequently, permit a non-invasive classification of the disease. Finally, this method may have a wide application due to its low costs, non-invasiveness and simple repeatability. This aspect is particularly interesting with respect to the social impact of the disease.

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